1296-016

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT OPERATION

In re application of:

Navin Vaya et al.

Serial No.: 10/630,348 Group Art Unit: 1615

Filed: July 29, 2003 Examiner: MERCIER, MELISSA S

For: **NOVEL DRUG DELIVERY SYSTEM**

Commissioner for Patents
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DECLARATION UNDER 35 U.S.C.§1.132

Sir:

I, Vinod Kumar Gupta am a named inventor in the above identified application and the following tests have been carried out at my direction:

Metformin tablets containing 750mg of metformin were prepared according to the general procedure of Example 8 of the above identified application using the following ingredients:

Component	Per Tablet (mg)	Per Batch (Kg)
GRANULATION		
Metformin Hydrochloride[(a)]	750.000	90.000
Lactose Monohydrate[(a)] (Pharmatose 200)	293.900	35.268
Ammonio methacrylate copolymer Type B (Eudragit RSPO)	114.000	13.680
Ferric Oxide Red	0.100	0.012
Methylene Chloride[(b)]	q.s.	9.380
Acetone[(b)]	q.s.	5.620
GRANULE COATING		
Hydrogenated Castor Oil	40.000	4.800
Methylene Chloride[(b)]	q.s.	64.194
LUBRICATION		
Magnesium Stearate	12.000	1.440
Total Theoretical Tablet Weight	**1210.00**	**145.200**

(a) The amount of Metformin Hydrochloride and Lactose Monohydrate listed above are the theoretical quantities based on an API assay value of 100%. Actual amount used are adjusted based upon assay results of API.

(b) Does not remain in the finished product, removed during the process.

The metformin tablets were tested by placing six tablets in separate vessels, that contained a sufficient amount of 6.8 phosphate buffer solution to cover the tablets, for time periods ranging from 2 to 12 hours. When the tablets were removed from the vessel after the stated period, excess water was removed with the help of tissue paper and the

photographs set forth below were taken with the same equipment that was positioned in the same manner for each sample:

Figure 1

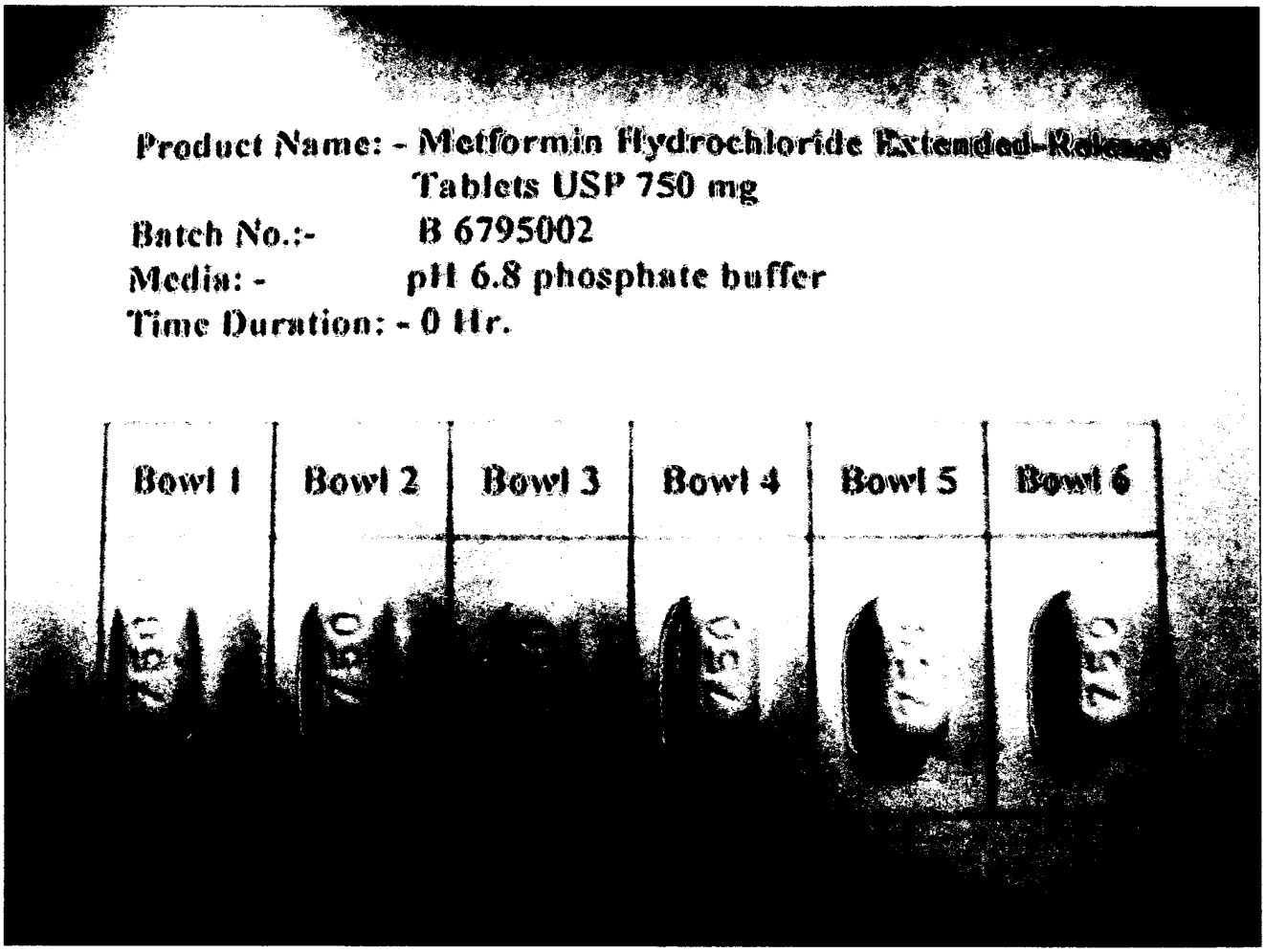


Figure 2

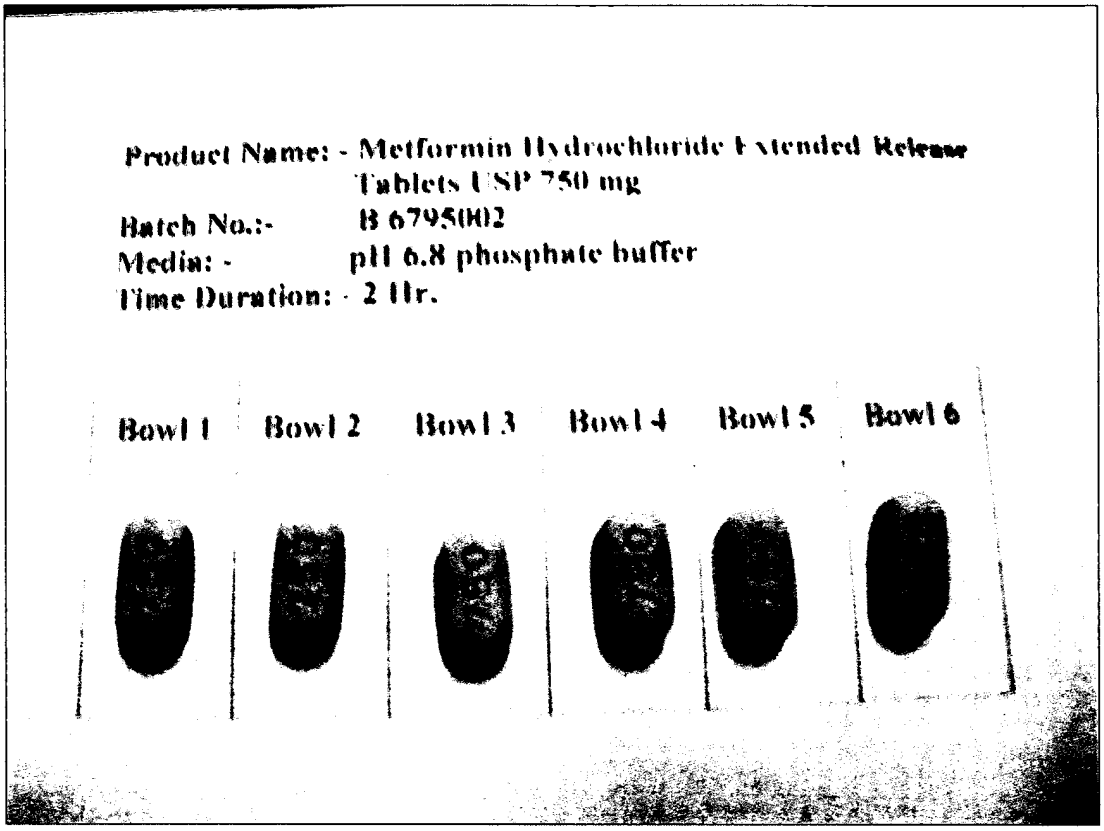


Figure 3

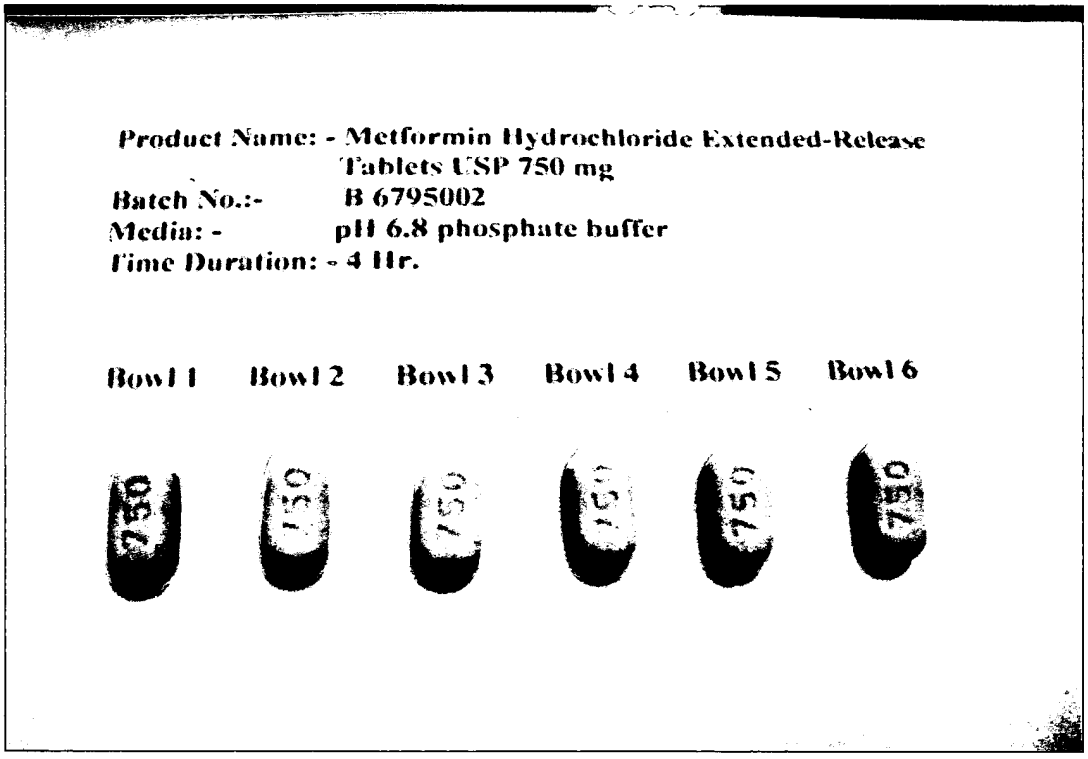


Figure 4

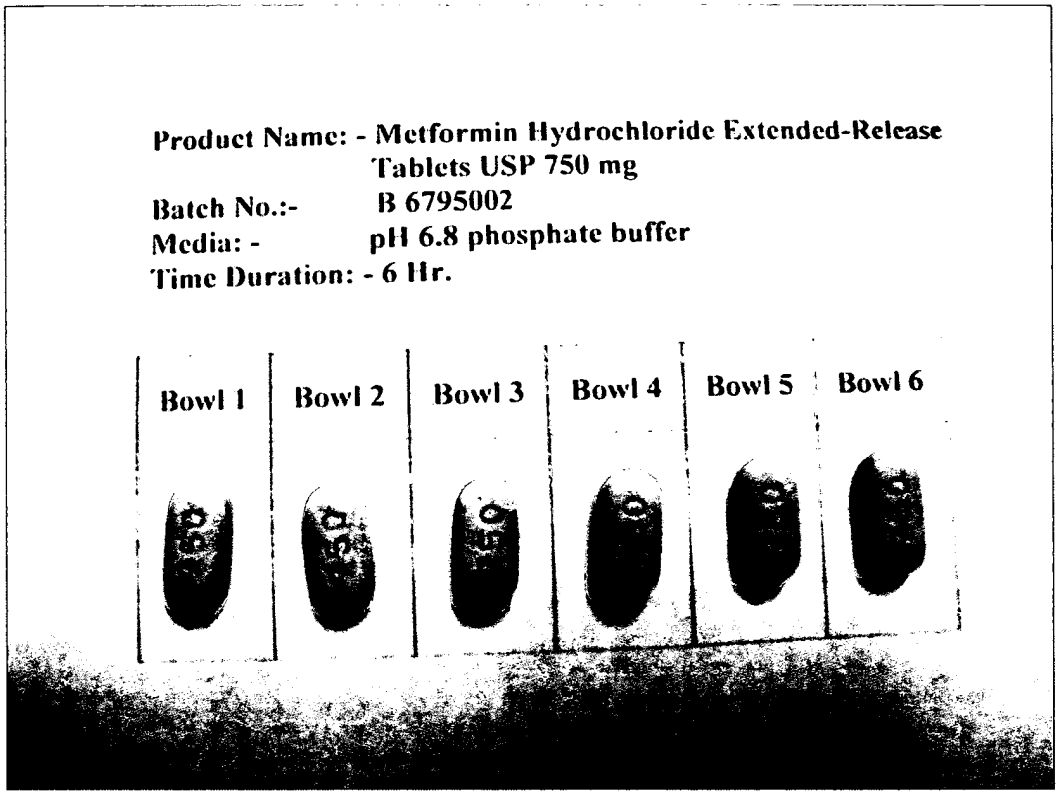


Figure 5

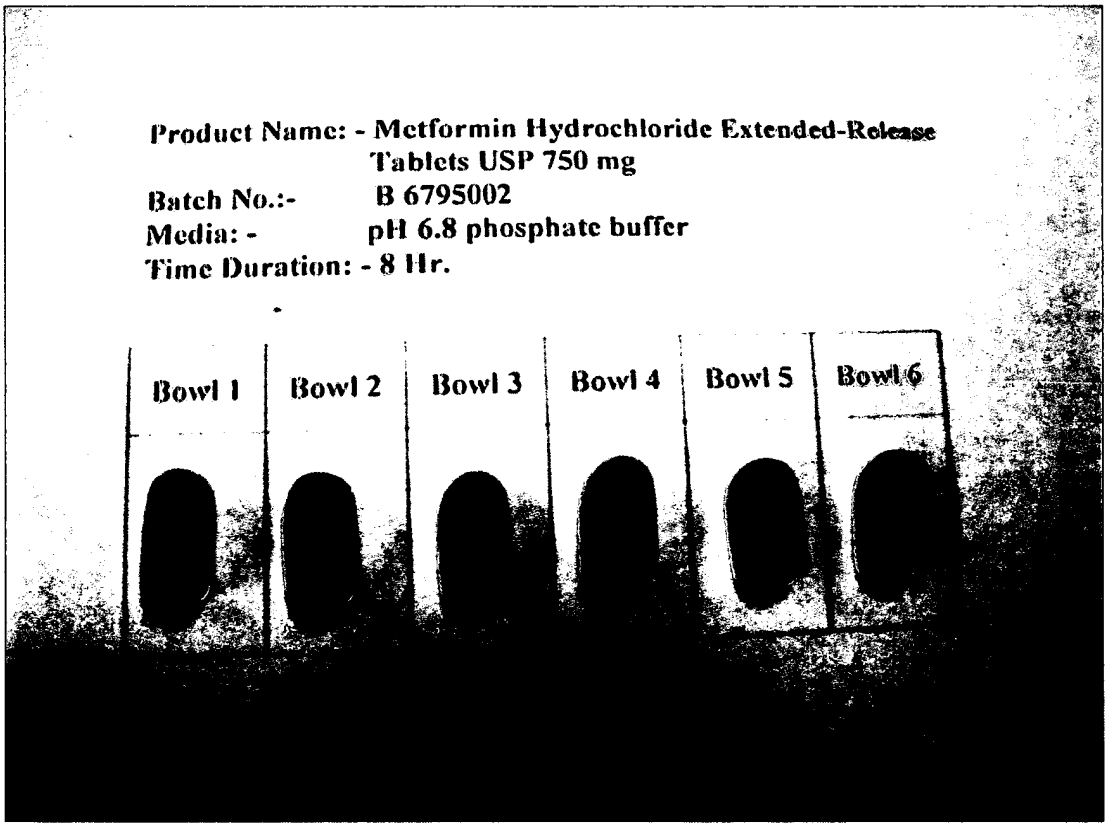


Figure 6

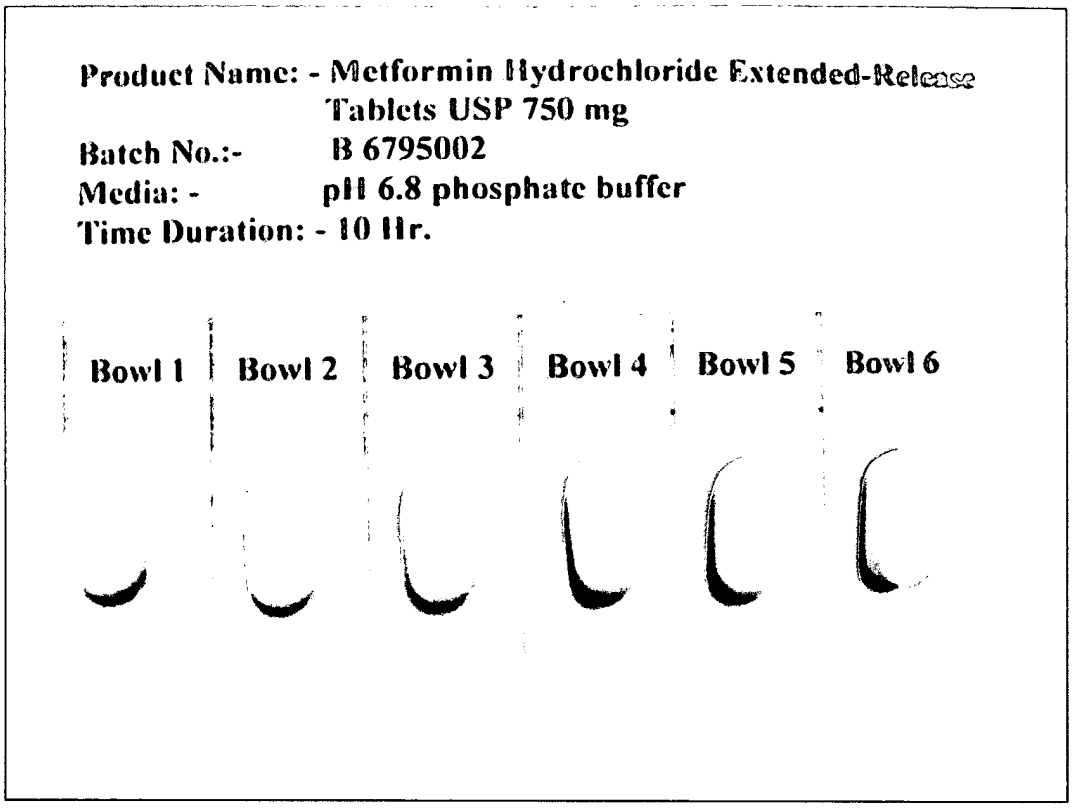
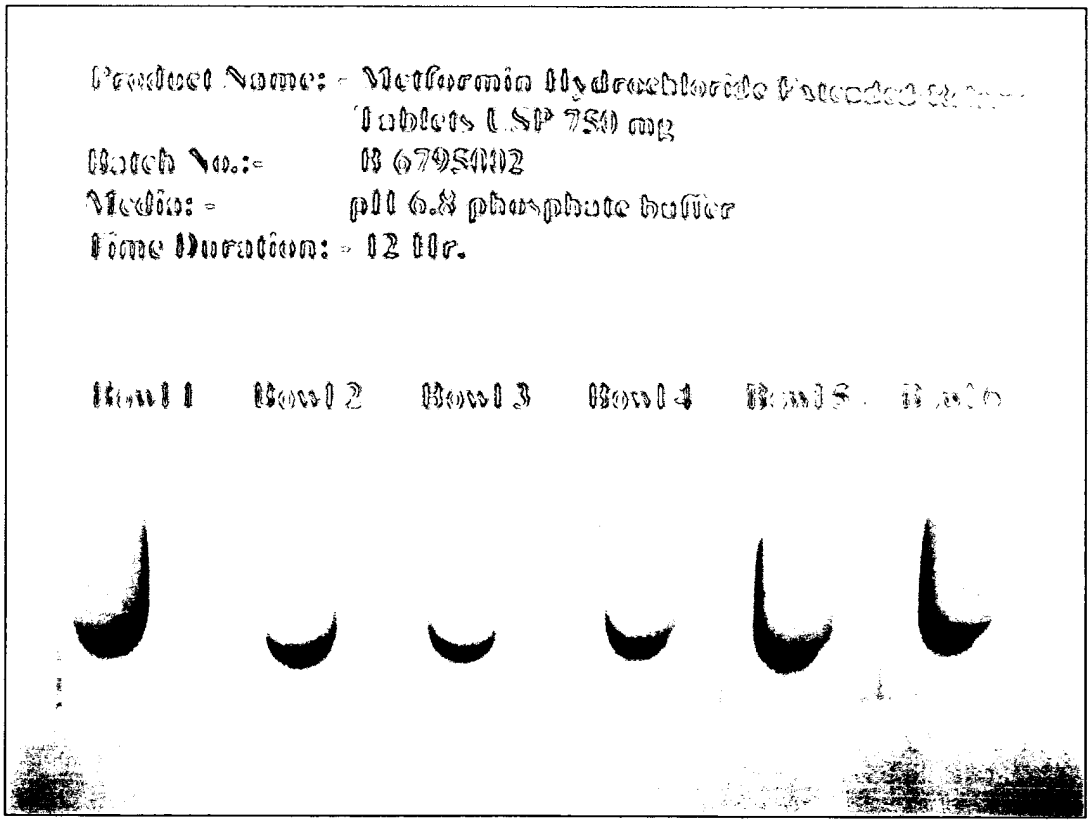


Figure 7



Inspection of the photographs of Figures 1-7 shows that there is no appreciable swelling of the tablets that could lead to the retention of the tablets in the stomach using the mechanism disclosed in U.S.6,600,300. The most important test is the comparison of the zero hour and two hour test photographs. The two hour time period exceeds the normal time for the passage of a pharmaceutical tablet through the human stomach and if a tablet does not swell during this period of time it does not have the swelling properties required by the dosage form of U.S.6,600,300 in order to prevent the dosage from passing rapidly through the stomach.

The following chart summarizes the dissolution of the metformin tablets of the invention in 0.1 N HCl and in pH 6.8 phosphate buffer:

Product	Media	Time Points										
		1 hr	2 hrs	3 hrs	4 hrs	5 hrs	6 hrs	7 hrs	8 hrs	9 hrs	10 hrs	12 hrs
Metformin HCl ER Tablets USP 750 mg (Batch No.: B6795002)	0.1 N HCl	40.4	54.9	64.3	65.1	79.1	--	88.0	—	95.0	—	99.4
	pH 6.8 phosphate buffer (New dissolution condition)	37.3	49.9	59.6	67.3	--	77.4	--	86.3	--	90.1	93.7

The dissolution tests show that the release of the metformin is substantially independent of the pH of the dissolution media which indicates that the rate of hydration of the metformin tablets of the invention, which is related to the swelling of the tablet under aqueous conditions, is also independent of the pH of the dissolution media.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and of any patent issued thereon.

Dated: 3rd July 2010

Vinod Kumar Gupta